REMARKS

Claims 1, 4-8, and 295-300 are pending in the application. Claims 2, 3, and 9-12 have been canceled. New Claims 295-300 have been introduced. Claims 13-294 have been withdrawn.

35 USC § 112 Rejections

Claim 1 is rejected under the second paragraph of 35 USC § 112 as being indefinite. According to the Office Action, the terms "first amine protecting group," "second amine protecting group," "functional group," and "strongly activated ester" are overly broad. The Office Action states that the Applicant can overcome the rejection by inserting specific groups.

Claim 1 has been amended to remove references to "functional groups" and "strongly activated esters." However, the Applicant respectfully submits that the term "amine protecting group" is well known in the art and clearly defined in the specification. At page 22, lines 8-20, the specification states that the "amine protecting group" may be any protecting group described in the book "Protective Groups in Organic Synthesis" by Theodora W. Greene and Peter G. M. Wuts, John Wiley and Sons publisher. Page 22, lines 14-18 of the specification state that preferred amine protecting groups include 9-fluorenylmethyl carbamate, allyl carbamate, benzyl carbamate, substituted benzyl carbamate, t-butyl carbamate, 1-adamantyl carbamate, 2-nitrobenzenesulfonyl, triphenylmethyl, (4-methoxyphenyl)diphenylmethyl, and 9-phenylfluorenyl. Because references to "functional groups" and "strongly activated esters" have been removed from Claim 1, and the term "amine protecting group" is clearly defined in the specficiation, Applicant respectfully traverses the 35 USC § 112, second paragraph rejection with respect to Claim 1.

Claims 1-8 are rejected under the second paragraph of 35 USC § 112 as being indefinite. According to the Office Action, the claims recite that R5 is N3 or NR2Y; it is not clear if applicants mean the N to be tertiary or if the 3 links include the pyrrolidine ring.

Claim 1 has been amended to recite that R_5 represents N_3 or –NH-Y. Basis for the language of amended Claim 1 is provided in the specification, e.g., at page 6, lines 23-25 and page 7, lines 1-12. Replacing "NR2Y" with –NH-Y clarifies that the N has

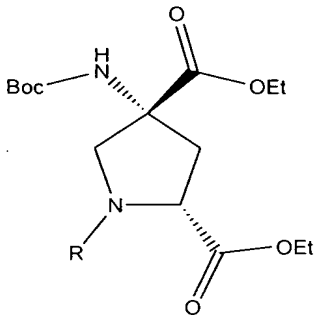
a total of three groups linked to it; it is not tertiary. N_3 is an azide. Thus, Applicant traverses the 35 USC § 112, second paragraph rejection with respect to Claim 1. Applicant also traverses the rejection with respect to dependent Claims 4-8, which include all of the limitations of independent Claim 1. Moreover, Claim 8 has been amended to recite a compound wherein R_5 is –NH-Y. Basis for the language of amended Claim 8 is provided in the specification, e.g., at page 6, lines 23-25 and page 7, lines 1-12. Claims 2 and 3 have been canceled.

Claims 1-12 are rejected under the first paragraph of 35 USC § 112 as failing to comply with the written description requirement. According to the Office Action, formula (1) indicates R5 to be N3 or NR2Y which would indicate that N has 4 groups attached to it making it tertiary. The Office Action states that the specification and the figures do not indicate it to be such; they all indicate that the N has a total of 3 groups linked to it.

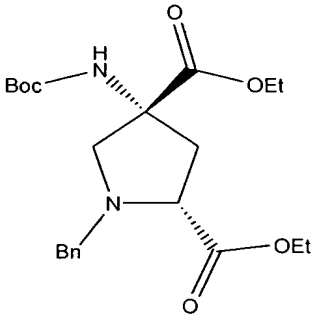
Claim 1 has been amended to recite that R_5 represents N_3 or –NH-Y. Basis for the language of amended Claim 1 is provided in the specification, e.g., at page 6, lines 23-25 and page 7, lines 1-12. Replacing "NR2Y" with –NH-Y clarifies that the N has a total of three groups linked to it; it is not tertiary. N_3 is an azide. Thus, Applicant traverses the 35 USC § 112, first paragraph rejection with respect to Claim 1. Applicant also traverses the rejection with respect to dependent Claims 4-8, which include all of the limitations of independent Claim 1. Moreover, Claim 8 has been amended to recite a compound wherein R_5 is –NH-Y. Basis for the language of amended Claim 8 is provided in the specification, e.g., at page 6, lines 23-25 and page 7, lines 1-12. Claims 2, 3, and 9-12 have been canceled.

35 USC § 102(b) Rejection

Claim 1 is rejected under 35 USC § 102(b) as being anticipated by Valli et al., "Synthesis and metabotropic glutamate receptor antagonist activity of N1-substituted analogs of 2R, 4R-4-aminopyrrolidine-2,4-dicarboxylic acid" (1998). According to the Office Action, the Valli et al. reference discloses compounds 6b-s and 4, depicted below, which read on the applicant's claimed compounds.



6b-s



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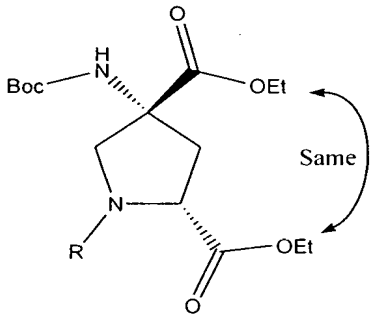
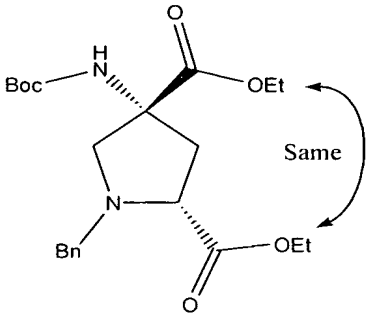
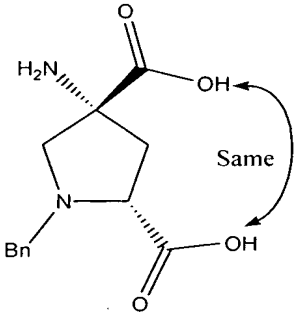
Applicant traverses the § 102(b) rejection with respect to Claim 1. The Valli et al. reference discloses compounds with identical carbonyl groups at the 2 and 4 positions. As shown below, the same carbonyl groups occur at positions 2 and 4 in compounds 6b-s, 4, and 7b-s of the Valli et al. reference.



6b-s



4



7b-s

In contrast, Claim 1 has been amended to recite compounds with different carbonyl groups at the 2 and 4 positions. According to Claim 1, R_6, which occurs at the 2 position, is a carboxylic acid. The carbonyl group at the 4 position, on the other hand, includes Z, which is a weak leaving group, e.g., a carboxy protecting group, alkoxide, thiolate, azide, or sulfonamide. Thus, for the presently claimed compound, the carbonyl group at position 2 will always be different than the carbonyl group at position 4. In contrast, the Valli et al. compounds will always have the same carbonyl groups at the 2 and 4 positions. As a result, it is submitted that the Valli et al. reference does not anticipate Claim 1 of the present invention. The 35 USC § 102(b) rejection is respectfully traversed.

35 USC § 103(a) Rejection

Claims 1-12 are rejected under 35 USC § 103(a) as being obvious in view of the Valli M. et al. reference. The Office Action states that Valli et al. discloses several compounds that have different N protecting groups than the presently claimed invention. However, according to the Office Action, there are several N-protecting groups known and since the function is the same one of skill in the art would find it obvious to use any of these groups.

Applicant traverses this 35 USC § 103(a) rejection with respect to Claims 1-12. Most of the difficulty in organic synthesis comes from differentiating functional groups with similar character from each other within a molecule. When identical functional groups are present on the same molecule, they become indistinguishable from one another during chemical transformations. In the Valli et al. compounds, the two carbonyl groups that are attached to the central five member ring always bear identical functional groups, either an –OEt group or an –OH group. This makes them indistinguishable from each other and any transformation that takes place on one will take place on the other. In the synthesis shown on page 1987 of the Valli et al. reference, treatment of compounds 6b-s with aqueous sodium hydroxide (step g) hydrolyzes both ethyl esters to carboxylic acids simultaneously.

For the compounds of the presently claimed invention, it is important to keep the two carbonyl groups distinct from each other at all times (see the specification at page 24, lines 4-12). Mild conditions and multiple step sequences are deliberately used to maintain different functionality on the two carbonyl groups. A special two step procedure is used to hydrolyze the hydantoin to a carboxylic acid so as to maintain the other carbonyl as a t-butyl ester. Then the carboxylic acid is methylated to form a methyl ester, leaving the t-butyl ester untouched. In the final step, the t-butyl group is removed from the t-butyl ester to reveal a carboxylic acid while leaving the methyl ester untouched. The resulting compound has one carboxylic acid and one methyl ester that acts as a carboxy protecting group. The compounds covered by Claim 1 have a weak leaving group at position Z while the other carbonyl group is a free carboxylic acid. Under the present invention, it is important for these two groups to be different because the carboxylic acid is the first point of attachment. The Valli

et al. synthesis would not produce the monomers of the presently claimed invention because the Valli et al. compounds have two indistinguishable carboxylic acids.

Based on the foregoing, it would not be obvious for a person of ordinary skill in the art to modify the Valli et al. compounds to obtain the compounds of the presently claimed invention. Valli et al. does not teach or suggest the use of two different carbonyl groups. In fact, Valli et al. teaches away from the use of two different carbonyl groups by only disclosing compounds in which the carbonyl groups are the same. There is no suggestion or motivation, either in the reference itself or in the knowledge generally available to those skilled in the art, to modify the Valli et al. reference to obtain Claim 1. Therefore, Claim 1 is not obvious in view of Valli et al., and the 35 USC § 103(a) rejection is traversed with respect to Claim 1. The rejection is also traversed with respect to dependent Claims 4-8, which include all of the limitations of independent Claim 1. Claims 2, 3, and 9-12 have been canceled.

Additional Claim Amendments

Several additional claim amendments have been made to clarify the scope of the invention.

Claim 1 has been amended to recite that X represents a first amine protecting group that is different from Y, and that Y represents a second amine protecting group that is different from X. Basis for the language of amended Claim 1 is located in the specification, e.g., at page 22, lines 18-19.

Claim 1 was also amended to recite that the stereochemical configuration at positions 2 and 4 is selected from the group consisting of (R,R), (R,S), (S,R), and (S,S). Basis for the language of this amendment is located in the specification, e.g., at page 6, lines 23-25, and page 7, lines 1-12.

In addition, Claim 5 was amended to recite that X is selected from the group consisting of benzyl-carbamate and t-Butyl carbamate. Basis for the language of amended Claim 5 is located in the specification, e.g., at page 6, lines 23-25, page 7, lines 1-12, and page 22, lines 8-32.

New Claims

Newly added Claim 295 recites a compound wherein X is t-butyl carbamate, Y is 9-fluoroenylmethylcarbamate, and Z is –OMe. Basis for the language of Claim

295 is provided in the specification, e.g., at page 6, lines 23-25, page 7, lines 1-12, and page 22, lines 8-32.

Newly added Claim 296 recites a compound wherein Z is selected from the group consisting of carboxy protecting groups, alkoxides, thiolates, azide, and sulfonamides. Basis for the language of Claim 296 is provided in the specification, e.g., at page 22, lines 21-32.

Newly added Claim 297 recites a compound wherein the first amine protecting group is selected from the group consisting of formyl, trityl, phenylfluorenyl, phthalimido, trichloroacetyl, chloroacetyl, bromoacetyl, iodoacetyl, benzyloxycarbonyl, 4-phenylbenzyloxycarbonyl, 2-methylbenzyloxycarbonyl, 4-methoxybenzyloxycarbonyl, 4-fluorobenzyloxycarbonyl, 4-chlorobenzyloxycarbonyl, 3-chlorobenzyloxycarbonyl, 2-chlorobenzyloxycarbonyl, 2,4-dichlorobenzyloxycarbonyl, 4-bromobenzyloxycarbonyl, 3-bromobenzyloxycarbonyl, 4-nitrobenzyloxycvarbonyl, 4-cyanobenzyloxycarbonyl, t-butyl carbamate, 2-(4-xenyl)-isoproboxycarbonyl, 1,1-diphenyleth-1-yloxycarbonyl, 1,1-diphenylprop-1-yloxycarbonyl, 2-phenylprop-2-yloxycarbonyl, 2-(p-toluyl)-prop-2-yloxycarbonyl, cyclopentanyloxy-carbonyl, 1-methylcyclopentanyloxycarbonyl, cyclohexanyloxycarbonyl, 1-methylcyclohexanyloxycarbonyl, 2-methylcyclohexanyloxycarbonyl, 2-(4-toluylsulfonyl)-ethoxycarbonyl, 2-(methylsulfonyl)ethoxycarbonyl, 2-(triphenylphosphino)-ethoxycarbonyl, fluorenylmethoxycarbonyl, 2-(trimethylsilyl)ethoxycarbonyl, allyloxycarbonyl, 1-(trimethylsilylmethyl)prop-1-enyloxycarbonyl, 5-benzisoxalylmethoxycarbonyl, 4-acetoxybenzyloxycarbonyl, 2,2,2-trichloroethoxycarbonyl, 2-ethynyl-2-propoxycarbonyl, cyclopropylmethoxycarbonyl, 4-(decyloxy)benzyloxycarbonyl, isobornyloxycarbonyl, 1-piperidyloxycarbonyl, benzoylmethylsulfonyl group, 2-nitrobenzenesulfonyl, 2-nitrophenylsulfenyl, and diphenylphosphine oxide. Basis for the language of Claim 297 is provided in the specification, e.g., at page 22, lines 11-13.

Newly added Claim 298 recites a compound wherein the first amine protecting group is selected from the group consisting of 9-fluorenylmethyl carbamate, allyl carbamate, benzyl carbamate, substituted benzyl carbamate, t-butyl carbamate, 1-adamantyl carbamate, 2-nitrobenzenesulfonyl, triphenylmethyl, (4-

methoxyphenyl)diphenylmethyl, and 9-phenylfluorenyl. Basis for the language of Claim 298 is provided in the specification, e.g., at page 22, lines 14-18.

Newly added Claim 299 recites a compound wherein the second amine protecting group is selected from the group consisting of formyl, trityl, phenylfluorenyl, phthalimido, trichloroacetyl, chloroacetyl, bromoacetyl, iodoacetyl, benzyloxycarbonyl, 4-phenylbenzyloxycarbonyl, 2-methylbenzyloxycarbonyl, 4-methoxybenzyloxycarbonyl, 4-fluorobenzyloxycarbonyl, 4-chlorobenzyloxycarbonyl, 3-chlorobenzyloxycarbonyl, 2-chlorobenzyloxycarbonyl, 2,4-dichlorobenzyloxycarbonyl, 4-bromobenzyloxycarbonyl, 3-bromobenzyloxycarbonyl, 4-nitrobenzyloxycvarbonyl, 4-cyanobenzyloxycarbonyl, t-butyl carbamate, 2-(4-xenyl)-isoproboxycarbonyl, 1,1-diphenyleth-1-yloxycarbonyl, 1,1-diphenylprop-1-yloxycarbonyl, 2-phenylprop-2-yloxycarbonyl, 2-(p-toluyl)-prop-2-yloxycarbonyl, cyclopentanyloxy-carbonyl, 1-methylcyclopentanyloxycarbonyl, cyclohexanyloxycarbonyl, 1-methylcyclohexanyloxycarbonyl, 2-methylcyclohexanyloxycarbonyl, 2-(4-toluylsulfonyl)-ethoxycarbonyl, 2-(methylsulfonyl)ethoxycarbonyl, 2-(triphenylphosphino)-ethoxycarbonyl, fluorenylmethoxycarbonyl, 2-(trimethylsilyl)ethoxycarbonyl, allyloxycarbonyl, 1-(trimethylsilylmethyl)prop-1-enyloxycarbonyl, 5-benzisoxalylmethoxycarbonyl, 4-acetoxybenzyloxycarbonyl, 2,2,2-trichloroethoxycarbonyl, 2-ethynyl-2-propoxycarbonyl, cyclopropylmethoxycarbonyl, 4-(decyloxy)benzyloxycarbonyl, isobornyloxycarbonyl, 1-piperidyloxycarbonyl, benzoylmethylsulfonyl group, 2-nitrobenzenesulfonyl, 2-nitrophenylsulfenyl, and diphenylphosphine oxide. Basis for the language of Claim 299 is provided in the specification, e.g., at page 22, lines 11-13.

Newly added Claim 300 recites a compound wherein the second amine protecting group is selected from the group consisting of 9-fluorenylmethyl carbamate, allyl carbamate, benzyl carbamate, substituted benzyl carbamate, t-butyl carbamate, 1-adamantyl carbamate, 2-nitrobenzenesulfonyl, triphenylmethyl, (4-methoxyphenyl)diphenylmethyl, and 9-phenylfluorenyl. Basis for the language of Claim 300 is provided in the specification, e.g., at page 22, lines 14-18.

Summary

Upon entry of this Amendment, Claims 1, 4-8, and 295-300 are believed to be in allowable form. The Applicant respectfully requests a Notice of Allowance.

In the event that any outstanding matters remain in connection with this application, the Examiner is invited to telephone the undersigned at 412-566-5941.

Respectfully submitted,

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